

Cardiology practice in the COVID-19 era

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As of 19 May 2020, there have been 4,805,000 confirmed cases of COVID-19 reported worldwide, with 318,000 fatalities. COVID-19 has placed an enormous strain on the healthcare systems where it has spread widely, with specific implications of the disease on cardiology practice. Indeed, infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative virus, primarily affects adults, with odds of death increasing both with age and comorbidities, including hypertension, diabetes, obesity and coronary artery disease.

Cardiovascular complications

In this issue of the *European Journal of Preventive Cardiology*, Ho et al.¹ provide an extensive review of 135 reports on coronavirus-linked diseases, severe acute respiratory syndrome (SARS), Middle East respiratory syndrome (MERS) and COVID-19, with a focus on associated cardiovascular issues. Cardiovascular comorbidities are commonly observed among patients admitted to hospital, associated with increased cardiovascular complications and fatality rates. Early clinical reports on COVID-19 show that about one-third of admitted hospital patients have any underlying cardiovascular disease (15%), hypertension (15%), or diabetes (20%), all associated with increased mortality rates (10.5%, 6% and 7.3%, respectively).^{1,2} Cardiac manifestations reported in patients with COVID-19 are common, and include myocarditis, acute coronary syndromes and arrhythmias either due to myocardial injury or treatment side-effects. Patients with cardiac injury, as defined as those with increased high-sensitivity troponin level, have a higher incidence of acute respiratory disease syndrome (ARDS) (58.5% vs. 14.7%, $P < 0.001$) and a higher mortality rate (51.2% vs. 4.5%, $P < 0.001$).³

Myocarditis has been reported with COVID-19 infection. In a series of 150 patients who died from the disease, death was attributed to myocarditis in 7%, and myocarditis was considered as having played a contributing role in 33% of them.³ The clinical

presentation of acute coronary syndromes in patients infected with the SARS-CoV-2 may be misleading. Among 18 patients who had ST-segment elevation indicating potential acute myocardial infarction, eight had obstructive coronary artery disease and 10 had non-coronary myocardial injury. Among them, 13 (72%) died in the hospital (four patients with myocardial infarction and nine patients with non-coronary myocardial injury).⁴ Cardiac arrhythmias are noted in 16.7% of 138 hospitalised patients in a Chinese cohort, and in 44% of those treated in an intensive care unit (ICU).⁵ Heart failure is also more common in patients admitted to ICUs and among non-survivors than among survivors.^{1–3,5} Accordingly, based on currently reported disease patterns extensively reviewed in the contribution by Ho et al.,¹ cardiovascular specialists are expected to be actively engaged in the care of patients with COVID-19.

Implications for healthcare systems and cardiology

There are numerous indirect effects of the current pandemic relevant to cardiovascular health and the organisation of cardiac care facilities which never happened previously. Cardiology practice is substantially modified by the COVID-19 outbreak. Many cardiac ICUs have been repurposed as medical or respiratory ICUs for the care of patients with COVID-19.⁶ Also, cardiologists are daily asked for advice in the departments of infectious diseases, ICUs and other medical facilities caring for patients with COVID-19 where they often spend more time than in their own department. Medical professionals caring for these patients are at

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high risk of contracting the infection. Aerosol-generating procedures such as non-invasive ventilation, high-flow nasal cannula and bag-mask ventilation are of particularly high risk. Appropriate personal protective equipment is required, with time-consuming dressing and undressing. Sometimes, shortages of gowns, gloves and surgical masks add a lot of difficulties and fears. In turn, staff shortages resulting from the infection of medical personnel may also affect patient care, as in our own institution where 90% of cardiologists have been infected simultaneously.

The COVID-19 pandemic directly impacts the management of cardiac patients in cardiac care units and cathlabs. To preserve hospital bed capacity, medical and paramedical staff resources and to avoid exposure of patients to the hospital environment, elective interventional procedures are restrained in many places.⁷ Exercising patients for non-invasive assessment using stress ECG or stress echocardiography is no longer performed in most instances, indications for transesophageal echocardiography are carefully weighed, and fewer patients are referred to cardiac rehabilitation units during follow-up.

Concomitantly, and yet not totally understood, the incidence of acute coronary syndromes referred to most coronary care units has decreased. Surprisingly, this was observed in areas where the disease has spread widely, but also in other areas less or not affected by the pandemic. Whereas this prevented hospital overcrowding during the first wave of the pandemic, concerns arose about the subsequent worsening of outpatients who have not received timely appropriate care.

Insights into pathogenesis

Novel insights into the mechanisms of cardiovascular complications of viral diseases have been highlighted during the current pandemic. The key role of the angiotensin-converting enzyme 2 (ACE2) as the cell receptor of SARS-CoV-2 and concerns about the safety of ACE inhibitors and angiotensin II receptor blockers (ARBs) administered to infected patients have reiterated research on mechanisms regulating ACE2 expression in the pathogenesis of hypertension and cardiovascular diseases.⁸ The debated use of hydroxychloroquine to block viral cell fixation has not only triggered a scientific controversy, but has also revisited the role of the terminal glycosylation of ACE2 allowing its activity.⁹

Cardiovascular complications of COVID-19 predominantly occur in the subgroup of severely ill patients, in whom hyperinflammation and multiorgan disease arise through excessive cytokine release from an uncontrolled immune activation.¹⁰ Patients with this

cytokine storm present with elevated D-dimers, rapid onset worsening, sepsis-induced coagulopathy (SIC) and ARDS. In addition, patients with markedly elevated D-dimers are at high risk of pulmonary embolism. In turn, anticoagulation appears to be associated with a better prognosis, both in patients meeting SIC criteria and in those with markedly elevated D-dimers.

Further challenges also arise from the recent reports of cases of Kawasaki disease in children infected with SARS-CoV-2, as Kawasaki disease, an acute vasculitis of childhood, is one of the leading causes of acquired heart disease in children, including cardiomyopathy and coronary involvement.¹¹

Faced with this new spectrum of cardiovascular diseases, cardiologists will have to develop novel practice approaches. This includes extensive follow-up of patients with related cardiovascular complications, as reported in the review by Ho et al.¹ It also includes patient care using innovative therapies such as interleukin inhibitors, antiviral drugs, antibodies from convalescent patients and monitoring them for potential cardiovascular side effects.¹²

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